Summing Up

Finally we discussed the good and bad aspects of the set-up. Pinkerleigh agreed that he was practising the kind of medicine he wanted to, without clinical interference, and that he would not change his job for anything. But, he thought, compared with the local general practitioners and other professional men, the consultants were poorly paid for the long hours they worked—especially the clinicians. What really irked him was the meanness of the authorities. No realistic payment was made for the many hours spent travelling to and from outpatients and domiciliary visits. No proper time allowance was made for the periods spent on dictating letters and notes, administration, and teaching. The refusal to pay for any domiciliary visits over 200 a year was grossly unfair, since they had to be made, often at inconvenient hours and in his spare time.

The thing that worried Dr. Pinkerleigh most was what the position would be in fifteen years' time; he doubted whether working conditions would get better and thought there were now objective signs that they were deteriorating. "I know many people might envy me this new hospital," he said. "The trouble is that as registrars we've been conditioned to work in nineteenth century slums. In fact, our kind of place should be what we—and the patients—expect as a right, as they do in Scandinavia and the States. Obviously, the present situation must be changed, but I think in this region they're going about it in the wrong way. They're trying to build four or five new district hospitals without the expertise or the resources. I've seen the existing slums at I, J, and K and I don't blame anybody for agitating for their replacement. But surely it would be better to concentrate on setting up a really first-class complete unit in one place and then move on to the next."

FOR DEBATE . . .

Impotence in Farm Workers using Toxic Chemicals

MICHAEL L. E. ESPIR,* M.A., M.B., M.R.C.P. ; J. W. HALL,† M.D., B.HY., D.P.H. ; J. G. SHIRREFFS,‡ M.B., CH.B.
DAVID L. STEVENS,§ M.B., M.R.C.P.

Summary: Four out of five members of a team of farm-workers who had been using various herbicides and pesticides in intensive agriculture became impotent. Sexual function recovered after further contact with the chemicals was stopped and hormone therapy had been given, though in one case this took about a year. We have not been able to incriminate one particular substance, but with the circumstantial evidence and the lack of any other obvious cause it seems likely that the impotence was due to the toxic effects of one or more of the chemicals being used.

Introduction

Impotence is unusual as an isolated symptom, and its occurrence in four out of five members of a team of farmworkers who were engaged in spreading chemicals strongly suggested a toxic cause. The men were working on a large estate using herbicides and pesticides as shown in the Table.

Substances Used on the Estate in 1967, Showing Purpose and Period of Use and Degree of Toxicity

Group of Compounds	Compound	Use	Season	Degree of Toxicity*
1. Organophosphorus ..	Malathion	I. A.	E. L.	+
	Thimet phorate	I.	E.	+ + +
	Morphothion	I.	E.	+
	Formothion	I. A.	E.	+
	Metasystox	I.	L.	+ + +
2. Substituted phenols ..	Dinoseb	H.	E. L.	+ + +
3. Dipyridyls	Paraquat	H.	E. L.	+ + +
4. Organochlorides	Dieldrin	I.	E. L.	+ +
5. Substituted phenoxy compounds	Dichloroprop	H.	E. L.	+
	2,4.D.	H.	E. L.	+
	M.C.P.A.	H.	E.	+
6. Triazines	Desmetryne	H.	E.	+
	Simazine	H.	E.	+
7. Carbamates	Barban	H.	E. L.	+
8. Dithiocarbamates ..	Mancozeb	Fu.	E. L.	+
9. Ureas and uracils ..	Urea with ammon, nitrate	Fe.	E. L.	+
	Linuron	H.	E. L.	+

H. = Herbicide. I. = Insecticide. A. = Acaricide. Fu. = Fungicide. Fe. = Fertilizer. E. = Early spring. L. = Late summer/autumn.
*Degree of Toxicity: + = slight, + + = moderate, + + + = severe. This is intended only as a rough guide and has been determined by reference to Edson (1955, 1960), Deichmann and Gerarde (1964), and Graham (1962).

Case Reports

Case 1.—The farm foreman, aged 46, was married and had one child. He was the first to consult one of us (J.G.S.) about three weeks after his symptoms began in April 1967. He complained of difficulty in achieving and maintaining an erection, having been previously normal in this respect. The possibility of a toxic cause was not suspected immediately, but fortuitously he stopped working with chemicals at this time. He was given methyltestosterone 5 mg. q.i.d. and had recovered completely within two months of the onset—that is, by June 1967. He was the least severely affected.

Case 2.—This man, aged 44, was the younger brother of Case 1. He was married and had five children, the youngest being born in 1964. In August 1967 he developed impotence, and three months later his wife sent him to see J.G.S. The symptoms were the same as in Case 1, and in view of their common occupation, a toxic cause was considered and he was advised to discontinue working with chemicals. He was also given methyltestosterone, and his symptoms cleared completely within three months.

Case 3.—The tractor driver, aged 37, was married and had one

* Consultant Neurologist, Regional Department of Neurosurgery and Neurology, Derbyshire Royal Infirmary, Derby.
† Medical Officer of Health, Barrow-upon-Soar Rural District Council.
‡ General Practitioner, Barrow-upon-Soar, Leicestershire.
§ Senior Registrar in Neurology, General Infirmary, Leeds.

child. In November 1967 he was sent by his wife to consult J.G.S. because of impotence, which had started in August. He was advised to stop working with chemicals and was started on treatment with methyltestosterone. He was referred to M.L.E.E. in February 1968, when he still had difficulty in achieving and maintaining an erection and ejaculation was delayed. He had never been ill before, he denied being depressed, and had no disturbance with micturition or sweating. Apart from the impotence he had no other symptoms, and clinical examination showed no abnormality. Improvement was gradual, but recovery took about a year to become complete.

Case 4.—This man, aged 35, was the brother of Case 3, but lived in a different area and consulted another general practitioner in August 1967. He had similar but less severe symptoms of impotence and was also treated with methyltestosterone. He recovered in two to three months.

Comment

The possibility that the impotence in these men might be due to chemicals being used on the farm was first suspected as soon as Case 2 presented, and when it was discovered that four of the five men were involved the Poisons Information Bureau at the Leeds General Infirmary was consulted. It was initially thought that the organophosphorus compounds were responsible, but we could not find any previous reports of impotence as an isolated manifestation. Serum cholinesterase was estimated in Cases 1, 2, and 3, but not until July 1968, and the results were normal.

It will be noted from the case reports that the impotence began in either April or August 1967. In Case 3 it began in April and got worse in August. Because of this observation an indication of the seasons when the various chemicals were used is given in the Table.

Subsequent inquiries revealed the following further details. The fifth member of the gang was a single man aged 19. He did not report any symptoms to his general practitioner (J.G.S.), but was not asked specifically about sexual function. An older brother of Cases 1 and 2 worked as a shepherd on the same farm, but he was not exposed to the chemicals and was not impotent at any time. The owner of the estate occasionally handled the chemicals but did not develop impotence. He enforced the regulations concerning the safe use of chemicals on the farm as specified by the Ministry of Agriculture (1966) and always took full precautions himself. The workers, however, occasionally disregarded them because of the discomfort from the lack of ventilation with the protective clothing. The tractor driver (Case 3) was in closest contact with the chemicals and he was the most severely affected.

The four men were regarded as "old-fashioned farm workers" and would be reticent about discussing their ailments among themselves. Each was unaware at the time that his colleagues were suffering from impotence. This being so, we feel that it is unlikely that their impotence was linked by any psychological chain reaction. It is also of interest that there was no appreciable fall off in their libido. Though each of the four men was treated with methyltestosterone, there is no clear evidence that this enhanced their recovery, which may have occurred spontaneously after they avoided further contact with the chemicals.

Discussion

Impotence with failure to achieve a satisfactory penile erection was the sole symptom in the four cases described. The peripheral nervous control of erection is mediated through the parasympathetic fibres of the nervi erigentes (S.2/3/4), and ejaculation by the hypogastric sympathetic nerves (L.2/3). Normal function is dependent on connexions with central nervous structures, including the cerebral cortex, temporal lobes, hypothalamic-hypophysial region, brain stem, and spinal cord. The causes of impotence have been reviewed by Johnson (1968), and can be classified as due to neurological, psychological, endocrinological, or local structural diseases or to toxic substances. Remission of the impotence, as occurred in the cases under discussion, is not consistent with many of the possible organic diseases, and though multiple sclerosis could not be excluded on this basis (Vas, 1969), there were no other manifestations of any neurological disorder in these men; neither was there any evidence of any psychological, endocrinological, or local structural disease.

Several reports on poisoning caused by the various chemicals listed in the Table have been published, but we have not been able to find any reference to impotence as one of the manifestations. Organophosphorus poisoning has been discussed by Edson (1955), Kleinman, West, and Augustine (1960), Rossiter (1960), Durham and Hayes (1962), and Hayes and Pirkle (1966). A farm worker with organophosphorus poisoning was also reported by Redhead (1968). We were informed that this patient, a bachelor and apparently disinterested in the opposite sex, was unsure whether he was impotent or not (Redhead, personal communication, 1969). The organophosphorus compounds produce toxic effects by inhibiting cholinesterase and acetylcholinesterase activity, thereby causing an accumulation of acetylcholine and eventually persistent depolarization at cholinergic nerve endings (Durham and Hayes, 1962; Sim, 1965). This would interrupt the reflex arc which produces erection, and likewise similar depolarization at the preganglionic sympathetic endings would interfere with ejaculation. It is possible that cholinesterase inhibition might also interfere with some modes of central nervous transmission; however, we have not found any previous report to suggest that any such mechanism could have a selective effect on sexual function.

With regard to possible psychological causes, Gershon and Shaw (1961) and Stoller, Krupinski, Christophers, and Blanks (1965) found no evidence that major mental illness resulted from exposure, even for long periods, to organophosphorus compounds. Furthermore, Durham, Wolfe, and Quinby (1965) showed that psychological deficits occurred only when there were acute manifestations of organophosphorus poisoning and that recovery was complete when normal cholinesterase activity was re-established. In view of this evidence, together with the apparent psychological normality of the men described here, it would seem unlikely that their impotence was due to a psychological disorder induced by organophosphorus poisoning.

The substituted phenol compound Dinoseb (dinitro-ortho-cresol, D.N.O.C.) causes its toxic effects by interfering with carbohydrate metabolism and increasing the basal metabolic rate (Edson, 1955), in fact producing a syndrome resembling thyrotoxicosis. Impotence can occur in thyrotoxicosis (Spence, 1953), but there was no other evidence of this in the present patients.

Paraquat is highly toxic, and acute poisoning can cause death by progressive pulmonary failure due to a proliferation of the bronchial endothelium (Bullivant, 1966; Almog and Tal, 1967; Campbell, 1968). Almog and Tal mentioned transient neurological signs in their patient. None of the recognized symptoms of paraquat poisoning occurred in our patients.

Dieldrin is a moderately toxic organochloride insecticide and can be absorbed through the skin. It causes central nervous stimulation by potentiating the activity of acetylcholine centrally (Deichmann and Gerarde, 1964). Acute poisoning leads to vomiting, muscle weakness, apprehension, coma, and convulsions. Minimal exposure causes headaches, anorexia, and nausea (Zavon, 1964). None of our patients had these symptoms. Poisoning with the substituted phenoxy compounds such as 2,4.D gives a clinical picture resembling dieldrin poisoning with the addition of paraesthesiae (Deichmann and Gerarde, 1964).

The carbamates are generally fairly safe compounds, but in large doses they can cause inhibition of acetylcholine, and can therefore produce a syndrome resembling organophosphorus poisoning.

This cluster of cases presented an unusual opportunity for investigation, as few farms have gangs of workers who might all be exposed to chemicals at the same time. Impotence in an isolated case is less likely to arouse suspicion of a toxic cause, so it was therefore fortunate that three of the men reported here had the same general practitioner. The natural reluctance of otherwise healthy men to complain of impotence may also account for the failure of some cases to come to light. We have inquired at several other large estates using chemicals to try to find out whether impotence was known to have occurred, but no similar cases had been heard of though one landowner thought that impotence was fairly common in farmworkers, probably due to "the long hours of work the fellows put in." The four men reported here were used to hard work and long hours and had not been impotent before. The farm had been converted from small tenancies into a large estate by removing hedges and ditches in order to develop a prairie-like expanse for intensive farming, and this was finally achieved by 1967. This then was the first year that the men had used the large quantities of chemicals over the entire area.

Having been unable to find any alternative cause, we have concluded that the reversible impotence in the men described here was probably due to the toxic effects of the chemicals to which they were exposed, even though they did not show any other recognized symptoms of poisoning with these compounds. Whether the symptoms were due to a single substance or to two or more compounds in combination has not been established, but we feel justified in reporting these cases along with details of the chemicals to which the men were exposed, in the hope that the cause may be clarified in the future if the possibility of impotence being a toxic effect of chemicals is borne in mind.

We are grateful to Mr. M. Ellis, Director of the Poisons Information Bureau, Leeds General Infirmary, Leeds, who suggested this investigation, and to Dr. I. M. Tuck, consultant pathologist at St. Margaret's Hospital, Epping, for the serum cholinesterase estimations. We should also like to thank Dr. Pamela M. Fullerton, consultant neurologist at the Middlesex Hospital, London, and M.R.C. Toxicology Research Unit, Carshalton, Surrey, for helpful discussion.

ADDENDUM.—Since submitting this paper a similar case has been mentioned in the *Medical News-Tribune* of December 19, 1969 (page 21). For the past three years a 35-year-old agricultural labourer complained of impotence, nausea, and some indigestion lasting about six weeks and starting in the middle of March. He himself was convinced that this was caused by the insecticide and herbicide sprays which he used at that time of year. The sprays which he thought upset him were Metasystox 55, Gesatop, and Tecane.

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